UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/464,039	12/15/1999	Rachel Meyers	5800-49	7067

826 7590 03/25/2002

ALSTON & BIRD LLP
BANK OF AMERICA PLAZA
101 SOUTH TRYON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	PAPER NUMBER
1636	13

DATE MAILED: 03/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/464,039	Applicant(s) MEYERS, RACHEL	
	Examiner S.Kaushal	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63-67,77-79 and 87-104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63-67,77-79 and 87-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 01/15/02 has been acknowledged.

Claims 61-62, 68-76 and 80-86 were canceled.
Claims 87-104 were newly filed.
Claims 63-65, 67 and 77-79 were amended.
Claims 63-67, 77-79 and 87-104 were pending and were examined in this office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The references cited herein are of record in a prior Office action.

► *If the claims are amended, added and/or canceled in response to this office action the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (http://www.uspto.gov) and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED.*

Claim Rejections - 35 USC § 101

Claims 63-67, 77-79 and 87-104 stand rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility, for the same reasons of record as set forth in the earlier official action mailed on the 08/19/01.

The applicant further argues that 21612 sequence (SEQ ID NO: 8) indicates that 21612 is a member of the short chain-dehydrogenase family of proteins based upon protein family domains analysis in PFAM database (response, page 7-8, ¶ 2). The applicant further argues that based upon homology to existing nucleic acid or proteins the invention as claimed assert a specific substantial and credible utility (response, page 8, ¶ 2).

However, this is found unpersuasive because PFAM analysis revealed that 21612 matches with a top-scoring domain for ADH-short but with a low sequence similarity. The specification fails to disclose that polynucleotide sequences of SEQ ID NO:8 encodes an amino acid sequence which is an human alcohol dehydrogenase (AHD) as shown by structural and/or functional properties. The recited SEQ ID NO(s) are simply computer-generated hypotheses, wherein no biological function has been established. It is known in the art that Alcohol dehydrogenase (ADH) constitutes a complex enzyme system with different forms and extensive multiplicity and the range of the biochemical reactions which can be catalyzed by ADH is extremely wide (Duester, Eur. J. Biochem 267:4315-4324, 2000, see page 4316 table 1, 2, page 4317-4319). The specification fails to show a single working example that establishes that the SEQ ID NO: 8 which encodes the amino acid sequence of SEQ ID NO:7 is a member of Alcohol dehydrogenase (ADH) family, such as by any substantial sequence homology and/or functional assay of the protein. The only immediate apparent utility for the instant invention would be its further scientific characterization as a putative ADH protein like activity.

Furthermore, One skilled in the art would not readily attribute any ADH-like activity encoded by the instant nucleic acid in view of the low sequence similarity and the lack of sequence conservation therein. At best the Office sequence search using the disclosed amino acid

sequences (SEQ ID NO:8) matches with a hypothetical protein belonging to ribitol-dehydrogenase super-family from C. elegans (ACC. No. T19954) and a human alcohol dehydrogenase (ACC. No. AA622988) but with only 41.7% and 12.7% sequence similarity respectively. Further inspection of the comparison shows limited if any areas of conservation between the two sequences. In view of such and the fact that ADH differs substantially in activity, it is unclear that any ADH-like activity could be attributed to the deduced amino acid sequence of the claimed nucleic acid sequences. Therefore, the asserted use for the claimed nucleic acid is not considered to support by either a specific and/or substantial utility, since no function can be ascribed to the gene.

Claim Rejections - 35 USC § 112

Claims 63-67, 77-79 and 87-104 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons of record as set forth in the earlier official action mailed on the 08/19/01.

The applicant argues that 21612 shares high level of sequence identity with consensus domain that is conserved among members of the short chain dehydrogenase family and the specification teaches methods for determining additional residues that are essential for the protein function. The applicant further argues that the specification provides guidance regarding

assays for dehydrogenase activity and one skill in the art would be able to determine the functionality of 21612 variants (response, page 10, ¶ 2-4).

However, this is found unpersuasive for the same reasons of record as set forth the lack of utility rejection above *(supra)*. The specification fails to show a single working example that establishes that the SEQ ID NO: 8 which encodes the amino acid sequence of SEQ ID NO:7 is a member of Alcohol dehydrogenase (ADH) family, such as by any substantial sequence homology and/or functional assay of the protein. It is unclear how one skill in the art would use the invention as claimed when the function of the polypeptide encoded by the nucleotide sequence of SEQ ID NO:8 is not known. In addition, the claimed invention is drawn to the polypeptide encoded by the nucleic acid sequences which hybridize to nucleic acid sequence of SEQ ID No:8 or have 70-90% sequence identity to SEQ ID NO:8 (see claims 88-90) The variants as claimed encompass 10-30% nucleotide sequence variation over the entire length of SEQ ID NO: 8. The variation also encompasses the conserved motifs that are germane to the ADH specific biological activity. The claimed invention is not enabled in view of lack of teachings in the specification as filed regarding what additional sequences may be added, deleted or substituted to those specifically disclosed, such that asserted utility discussed in the section 101 rejection above would be recognized as specific and/or substantial. The specification as filed only teaches nucleic sequence of SEQ ID NO:8 which encodes the amino acid sequence of SEQ ID NO:7 and it is not even clear whether the SEQ ID NO:8 encodes any alcohol dehydrogenase like activity. In addition, the specification fails to disclose that any and all variants of SEQ ID NO:7 (as claimed) are capable of eliciting any ADH-like activity.

It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The recited SEQ ID NO(s) are simply computer-generated hypothesis because no biological function has been established. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. Therefore, applicant has not presented enablement commensurate in scope with the claims.

In addition, the specification fails to disclose the role of the claimed polypeptides encoded by SEQ ID NO: 8 in any disease. It is unclear whether the disease would be the result of the loss of 21612-like activity or is the result of altered protein function. It is even unclear whether the treatment of the disease associated with polypeptide as claimed would require increase or decrease in the expression of claimed 21612 protein. Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed. The quantity of experimentation required would include the functional characterization of polypeptide encoded by SEQ ID NO: 8 as a protein having an alcohol dehydrogenase-like activity and use thereof.

In addition the invention as claimed encompass a host cells in vivo which contains the claimed nucleic acid sequences (see claim 65-67 and 95-97). The applicant argues that vectors and methods of gene therapy and for the production of transgenic animals are well known to those skill in the art andy many factors that determine the success of the methods have been

identified (response, page 11, ¶ 3). However, this is found unpersuasive because Applicant's argument alone cannot take place of evidence lacking in the record. The art at the time of filing clearly teaches that the Gene therapy is considered highly experimental area of research at this time, and both researchers and the public agree that demonstrable progress to date has fallen short of initial expectations (Rosenberg et al, Science 287:1751, 2000). Similarly, the state of transgenic art at the time of filing was such that phenotype of an animal is determined by a complex interaction of genetics and environment. (Wood. Comp. Med. 50(1): 12-15, 2000, see page12). In addition, the scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Claims 88-92 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The applicant argues that invention as claimed has been described by both structural and functional properties (i.e. dehydrogenase activity), thereby meets the standard set forth in the "Written description" guidelines. However, this is found unpersuasive because the applicant fails

to point out where in the specification it is disclosed that the polypeptide encoded by the nucleic acid molecule of SEQ ID NO: 8 have any alcohol dehydrogenase-like activity explicitly or implicitly as putatively consider by the applicant. The instant claims are drawn to a nucleotide sequence encoding a polypeptide having dehydrogenase activity, wherein the nucleotide has at least 70-90% sequence identity with nucleotide sequence of SEQ ID NO:8. The specification as fails to disclose any and all variant of human alcohol dehydrogenase comprising the nucleic acid sequence of SEQ 8, which encodes the amino acid sequences of SEQ ID NO:7. The specification discloses only one variant of ADH-like polypeptide within the scope of genus comprising the claimed SEQ ID NO:8. The specification proposes to discover other members of the genus using hybridization procedure. However, there is no description of mutational sites that exist in nature, and there is no description how the structure of identified nucleic acid sequences relates to the structure of any strictly neutral alleles. The art at the time of filing teaches that ADH-like polypeptides include members that would be expect to have widely divergent functional properties based upon their substrate specificity (Duester, Eur. J. Biochem 267:4315-4324, 2000, see page 4316 table 1, 2, page 4317-4319). At best the specification only disclosed nucleic acid sequence of SEQ ID NO: 8 which encodes the amino acid sequence of SEQ ID NO:7. The specification fails to disclose any and all variants of nucleic and amino acid sequences of SEQ ID NO(s) as claimed. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claim 79 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 79 is indefinite because it is unclear what are the "instructions for use" in this context. The applicant fails to address this rejection in the response filed on 01/15/02.

Conclusion

No claims are allowed.

Claims 63-67, 77-79 and 87-104 are free of prior art of record. The prior art does not teach or suggest nucleotide sequence of SEQ ID NO: 8 which encodes a human alcohol dehydrogenase of SEQ ID NO:7.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Irem.Yucel can be reached on (703) 305-1998. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Zeta Adams, whose telephone number is (703) 305-3291.

S. Kaushal
Patent examiner

Scott D. Priebe
SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER